Management of the Compressible Multi-Nodular Goitre
Doncaster 2012
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Whipps Cross Hospital
What is a goitre?

► Normal thyroid gland: 10-25g
► Goitre: from Latin: *guttur* = throat
► WHO: a thyroid whose lobes have a vol. > terminal phalanges of the thumb of the person being examined
► Lifetime risk of nodule = 10%
  □ ↑ in women, ↑ age, radiation exposure & iodine deficiency
► Multinodular goitre: most common cause of thyroid enlargement
Multinodular Goitre

► Sporadic
  □ most common cause of nontoxic goitre

► Diet
  □ Iodine deficiency $\rightarrow \uparrow$ TSH
  □ Brassica (cabbage, turnips, cauliflower, broccoli) block T4 formation
  □ Cassava: contains thiocyanate

► Familial
Multinodular goitre (MNG)

► Prevalence in UK*
  □ Small goitre 9% (palpable not visible)
  □ Obvious goitre 7% (palpable & visible)
  □ F:M = 4:1 (UK)

Clinical features

- Functional
  - Hyper/Hypo thyroidism
- Cervical
- Retrosternal
- Non compressive
- Compressive
  - Laryngeal deviation
  - Tracheal compression/deviation
  - Oesophageal compression
  - SVC Obstruction
Retrosternal Goitre

First described by Haller in 1749

► Definition
1. Descends below the plane of the thoracic inlet
2. > 50% below the plane of the thoracic inlet
3. Intrathoracic extension requiring reaching into the mediastinum for dissection
4. Anterior-superior mediastinum extension > 2cm
5. Reaching the 4th thoracic vertebra

► Female: Male 4:1

► Incidence
1. 0.02 to 0.5% (CXR)
2. 0.05% of females > 40 years
3. 3-12% of mediastinal masses
4. 1-20% of patients requiring thyroidectomy


MNG-Symptoms/Signs

► Stridor, OSAS, Dyspnoea on lying flat
► Dysphagia
► Cosmesis
► Pemberton’s sign (facial plethora, cyanosis and distension of neck veins, when raising both arms simultaneously {Pembertons manoeuvre!}).

Seen in thoracic inlet obstruction originally described in patients with retrosternal goitre may also be seen in lung carcinoma, lymphomas, thymomas, dermoid cysts or aortic aneurysms

► SVC syndrome
► Ankle oedema
► Hypertension (reversed with surgery)

Pathology

- Variably and irregularly enlarged gland
MNG Malignancy Risk

- Nodules of MNG undergo malignant change at similar rates to other thyroid tissue.
- Risk: 1 in 20
  - Wadström 1999 4-8%
  - Miccoli 1993 8%
  - Gandolfi 2004 14%
  - Yamashita 1997 31% (54% of those >1 cm)
Factors suggesting malignancy

► **Moderate risk**
- Age <20, >60
- Male
- Solitary nodule
- Irradiation
- Compressive symptoms
- Hashimoto’s
- Genetic factors

► **High risk**
- Rapidly enlarging painless mass
- Increases with age
- Fixation
- Hoarseness
- Cystic Lymphadenopathy: levels 2/3/4
- Previous Thyroid ca
- Family history
- Family history: MEN 2a/b
• 55 male from Ukraine
• 18/12 lymphadenopathy
• Aspirate: 20mls thin black fluid

• Papillary ca on FNAC
Investigation Compressive MNG

- US
- FNAC
- TFT’s
- Autoimmune antibodies
- CT (?Malignant – non contrast)
- Resp Function tests
  - Flow volume loops
- FBC, ECG, Ca2+ etc

- Consider calcitonin
  - Not for screening
  - Family history
- RET proto oncogene
  - in up to 60% PTC
  - in up to 75% follicular variant PTC
  - in 33% sporadic MEN
  - in 95% MEN2A
- **No role: Scintography**
  - BAETS 2002
  - ATA 1996

Thomas GA et al. High prevalence of RET/PTC rearrangements in Ukrainian and Belarussian post-Chernobyl thyroid papillary carcinomas: A strong correlation between RET/PTC3 and the solid-follicular variant. Journal of clinical endocrinology and metabolism. 1999;84:4232-8
CT/MR

- Retrosternal extension
- Tracheal deviation (preop), intubation planning
- Tracheal compression
  - Note variation in tracheal diameter with respiration and patient position
Treatment of MN or Diffuse Goitre

Conservative
- Nil treatment
- Cyst aspiration

Thyroid suppression
- Thyroxine
- Anti Thyroids
  - Propylthiouracil & Methimazole

Radioiodine Ablation
- I-131

Surgery
- Hemi-thyroidectomy
- Total Thyroidectomy
  - Subtotal Thyroidectomy
  - Near Total Thyroidectomy
Non surgical treatment

► Elderly patients because of cardiac, pulmonary or other disabling disorders
► High risk patients
► Patients who decline surgery
► Smaller nodules
► Patients had previous surgery
► Recurrent laryngeal nerve injury

Howarth DM et al. Outpatient management of patients with large multinodular goitres treated with fractionated radioiodine. European Journal of Nuclear Medicine and Molecular Imaging, Volume 24, Number 12 / December, 1997
Thyroxine Suppression

Thyroxine $\rightarrow\downarrow$ TSH $\rightarrow\downarrow$ gland stimulation

- Recommendation: TSH 0.1-0.5mU/L
- Efficacy: Numerous small series suggest efficacy
- No additional benefit with carbimazole
- Less effective in larger goitres.

► Risks:

- Growth of nodules resumes on ceasing suppression. Therefore treatment is life long
- Subclinical hyperthyroidism
- Reduced bone density and accelerated loss in Pre/Post MP women
- Increased LV Mass ?significant.
- AF
- Level of suppression not well defined

Radio-Iodine

- **Response rates 65-99%**
- **Improvement of dysphagia or dyspnoea in 70% - 90%**
- **Volume reduction**
  - 40% at 1 yr
  - 50-60% at 3-5 yrs
  - Slowly produces tracheal widening and ↑ Respiratory Function
- **Tracheal cross sectional area ↑ = 36%**
- 18 months post treatment, 66% were hypothyroid.
- **Excellent short- and medium-term safety, well tolerated**
- **Satisfactory alternative treatment to surgery**

Howarth DM et al. Outpatient management of patients with large multinodular goitres treated with fractionated radioiodine. Eur J Nuc Med & Mol Imag, 24 (12) 1997 Dec,
Thyroid volume (left), maximal deviation of the tracheal center from the midline (middle), and smallest cross-sectional area of the tracheal lumen (SCAT) (right) measured before and 1 year after radioiodine therapy in 19 patients with a large, compressive multinodular goiter.


Patient 17 before and 1 yr after treatment
Radio-Iodine Risks

- Acute thyroiditis (enlargement) further compressing the trachea
  - ? prednisolone
- Induction of thyroid malignancy (lifetime risk 1.6%)
- Variable response
- High treatment failure
- Transient hyperthyroidism
- Post Ablation Hypothyroidism (up to 50% at 5 years)
  - Higher with rhTSH
    - 23.5% group 1
    - 64.0% group 2 at 12 months
- Local cervical pain
- Loss of taste
- Oesophagitis
- Sialoadenitis
- Transitory leukopaenia
- Weight loss
- Away from children for 2 weeks
- Autoimmune hyperthyroidism-Graves-like (5%)
- Recurrence 10% at three to five years
  - Second dose may be effective
Theodor Kocher 1841 - 1917

- The Nobel Prize in Physiology or Medicine 1909
- Trained by Demme, Lücke, Billroth, and Langenbeck
- His book *Erkrankungen der Schilddrüse* (Diseases of the thyroid gland) discussed the aetiology, symptoms and treatment of goitres.
- 5000 career thyroidectomies
- Mortality rates decreased
  - 40% in 1850 (pre-Kocher & Billroth)
  - 12.6% in 1870’s (Kocher begins practice)
  - 0.2% in 1898 (end of Kocher’s career)
  - Attention to asepsis
- Many patients developed cretinism or myxoedema
  - His conclusions in presentation to the German Surgical Congress in 1883 ...
  - “...the thyroid gland in fact had a function....”
Figure 21-19. The dramatic case of Maria Richsel, the first patient to have come to Kocher’s attention with postoperative myxedema following total thyroidectomy. A. The child and her younger sister before the operation. B. The changes nine years after the operation. The younger sister, now fully grown, contrasts vividly with the dwarfed and stunted patient. Also note Maria’s thickened face and fingers, which are typical of myxedema. Because of this and other patients with the same problem, Kocher stopped performing total thyroidectomies. For this work, demonstrating the physiological importance of the thyroid gland in humans, Professor Kocher was awarded the Nobel prize. From: Kocher T. Uber Kropfextirpation und ihre Folgen, Arch Klin Chir 29:254, 1883, with permission.
MNG-Surgery

- **Indications**
  - Cosmesis
  - Compressive Symptoms
  - OSA
  - Suspicion of Malignancy
  - Retrosternal Goitre
  - Thyrotoxicosis
Hemi-thyroidectomy

- For unilateral cosmesis (MNG), solitary nodule, Thy 3, U/S concern etc
  - Low risk of...
    - Hypothyroidism
    - Perm Hypoparathyroidism
    - RLN injury
  - Risk of progressive contra-lateral disease (MNG)

Total Thyroidectomy

- Complete excision of the gland bilaterally.
- Lifelong Thyroxine replacement.
- **Nil risk of recurrence**
- Recommended rather than subtotal/Near total thyroidectomy for MNG and Graves


# Thyroidectomy

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Near Total</th>
<th>Subtotal</th>
</tr>
</thead>
<tbody>
<tr>
<td>HypoCa^{2+}</td>
<td>Low risk (Transient 7%)</td>
<td>Low risk</td>
<td>Low risk</td>
</tr>
<tr>
<td>RLN injury</td>
<td>Low risk 1%</td>
<td>Low risk 1%</td>
<td>Low risk 1%</td>
</tr>
<tr>
<td>Recurrence</td>
<td>0</td>
<td>Low risk</td>
<td>Higher risk (25%)</td>
</tr>
<tr>
<td>Second operation</td>
<td></td>
<td></td>
<td>Higher risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Increased morbidity</td>
</tr>
<tr>
<td>HypoT4 (Graves)</td>
<td>100%</td>
<td>92%</td>
<td>29%</td>
</tr>
<tr>
<td>Hyper T4 (Graves)</td>
<td>0</td>
<td>0</td>
<td>34% (Treatment fail)</td>
</tr>
<tr>
<td>Compressive MNG</td>
<td>Treatment of choice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graves</td>
<td>Treatment of choice</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Preop Assessment

► Airway issues
► Need for sternotomy: Rare
► Where is surgery best undertaken?
Aberrant Intrathoracic Thyroid

- Operative approach completely different
- Thoracotomy
- Blood supply intrathoracic Not cervical

Guidelines

► Revised ATA Guidelines for Patients with Thyroid Nodules & DTC 2009
► Guidelines for the management of thyroid cancer 2nd ed 2007 BTA & RCP
► European Association of Nuclear Medicine consensus guidelines for RAI therapy of differentiated thyroid cancers 2008
► ATA Statement on Essential Elements of Interdisciplinary Communication of Perioperative Information for Patients Undergoing Thyroid Cancer Surgery 2012
► Guidelines of the ATA for Diagnosis & Management of Thyroid Disease During Pregnancy & Postpartum 2011
► Radiation Safety in the Treatment of Patients with Thyroid Diseases by Radioiodine \(^{131}\)I: Practice Recommendations of the American Thyroid Association 2011
► ATA Consensus Statement on Terminology & Classification of Central Neck Dissection for Thyroid Cancer 2009
► American Thyroid Association Design and Feasibility of a Prospective Randomized Controlled Trial of Prophylactic Central Lymph Node Dissection for Papillary Thyroid Carcinoma 2012
► UK Guidelines for the Use of Thyroid Function Tests 2006
► Guidelines for the Surgical Management of Endocrine Disease and Training Requirements for Endocrine Surgery 2003
► Paediatric Endocrine Tumour Guidelines
The Problem

► **Nodule: Common**
  - palpable 5% ♀ 1% ♂
  - ultrasound 20-67%

► **Ca: 10%**

► **Risks:** age (<10 - >40), sex (male), radiation (childhood/Chernobyl), FHx (ca & adenoma), endemic goitre, Cowden’s syndrome, familial adenomatous polyposis

► **DTC: 90%:** papillary (PTC)/follicular cancer (FTC)

Cowden’s syndrome: macrocephaly, mild learning difficulties, carpet-pile tongue, with benign or malignant breast disease
Incidence UK

- 1% of all malignancies, most common endocrine tumour
- Increasing incidence
- 1971–95
  - 2.3/100,000 women
  - 0.9 per 100,000 men
  - 900 new cases/year
  - 250 deaths/year
- 2001
  - 3.5/100,000 women
  - 1.3/100,000 men
  - 1,200 new cases/year
- PTC due to use of US, FNAC and early treatment
  - 50% of the in ca < 1cm
  - 90% of the in ca < 2 cm
Diff Thyroid Ca Management

- Specialist multidisciplinary team (MDT)
- Regional cancer network
- Timeframe complying to DoH targets
- One stop clinic
- Surgeon, endocrinologist, oncologist (or nuclear medicine physician), pathologist, dedicated radiologist, specialist nurse etc
- Combined clinic, Databases, BAETS audit
- Patients
  - seen by one or more members of the MDT
  - have a key-worker
  - Access to education, support etc
Aim of Management of DTC

- Accurate pre-op staging
- **Removal of primary**: Total thyroidectomy (Hemi: small/low risk)
- **Treatment of locoregional disease** (even in metastatic disease)
- Minimal morbidity
- Post operative staging and prognosis
- Postoperative treatment with radioactive iodine
- **Long-term surveillance for disease recurrence** (RAI whole-body scanning (WBS) and serum Tg)
- Education & Support (Key worker)
US Thyroid nodule & FNAC

► Need Dedicated Radiologist
► Suspicious features
  - *Microcalcifications*
  - marked hypoechogenicity
  - irregular margins
  - absence of a hypoechoic halo around the nodule
  - extracapsular extension
  - *local invasion of adjacent structures*
  - lymphadenopathy
  - number, size, and *interval growth* of nodules
► US guided FNAC of suspicious thyroid nodules
  - inadequate fine-needle aspirates
Microcalcification

- 30%–60% of all primary thyroid ca
- most commonly in PTC
- Also FTC & anaplastic ca as well as in benign conditions (follicular adenoma & Hashimoto thyroiditis)
- US: punctuate hyperechoic foci without acoustic shadowing
- **psammoma** bodies
  - 10–100-μm round laminar crystalline calcific deposits
  - specific feature of thyroid ca
    - specificity of 85.8%–95%
    - positive predictive value of 41.8%–94.2%
Transverse ultrasound of the right lobe of the thyroid demonstrates punctate echogenic foci without posterior acoustic shadowing, findings indicative of microcalcifications (arrows).
Photomicrograph (original magnification, × 400; hematoxylineosin stain) shows a psammoma body (arrow), a round laminar crystalline calcification.
Papillary carcinoma in an 87-year-old man. Transverse sonogram of the thyroid isthmus shows a poorly defined tumor with marked hypoechogenicity and irregular margins (arrows) and without a hypoechoic halo.

Hoang J K et al. Radiographics 2007;27:847-860
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Interval Growth

► Serial US examinations 6–18 months
  □ Same radiologist, recorded images
  ○ Stable: Scan every 3–5 years
    □ < 50% change in volume
    □ < 20% change in nodule dimensions

► Growth: Repeat US guided FNAC
  □ > 50% change in volume
  □ > 20% change in nodule dimensions
  □ Minimal increase of 2 mm $V = \frac{4}{3} \pi r^3$
US central & lateral nodes & FNAC

- US guided FNA of suspicious lymph nodes
- Suspicious nodes: 20% (! △ in op)
  - Loss of the fatty hilus: high sensitivity
  - Peripheral vascularity (instead of just normal central hilar vessels): high specificity
  - Round bulging shape
  - Increased size
  - Cystic areas
  - Heterogeneous echotexture
  - Microcalcification
  - Irregular margins

- US guided lymph node FNAC with Tg washout
- Black cystic fluid: Papillary met!!! (send all fluid)

- Post op
  - Histologically +ve nodes: 20-50% (papillary)
  - Micromets: up to 90%
Papillary carcinoma and cystic lymph node metastasis in a 28-year-old woman

(a) Longitudinal sonogram of the right lobe of the thyroid shows an irregular hypoechoic tumor with microcalcifications. (b) Longitudinal sonogram of the right neck shows a cystic level 5 nodal metastasis with internal septation and foci of calcification (arrows). (c) Axial contrast-enhanced CT image shows the metastasis (arrow).

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Neck Mets: CT
FNAC (Thy 1 – 5)

- Thy 1 Non-diagnostic  
  - repeat: US guided
    - Cysts: colloid or histiocytes only, without epithelial cells, Aspirated to dryness with no residual mass, clinical/ultrasound follow-up

- Thy2 Non-neoplastic  
  - Two non-neoplastic results 3–6 months needed to exclude ca
    - High risk  
      - Lobectomy

- Thy3 Suspected follicular neoplasm: Lobectomy

- Thy4 Suspicious of malignancy (suspicious, but not diagnostic, of papillary, medullary or anaplastic carcinoma, or lymphoma).
  - ? Repeat (for Thy 5)
  - MDT discussion
  - Surgery

- Thy5 Diagnostic of malignancy
  - MDT discussion
  - Further investigation
  - Surgery: Total thyroidectomy
Preop staging with diagnostic imaging & laboratory tests

► TFT & Ca

► CT (non contrast), MRI & PET

- Not recommended routinely
- Assessment of large, rapidly growing, retrosternal or invasive tumours
- MRI can be useful for ? retropharyngeal nodes
What is the appropriate op for indeterminate thyroid nodules & DTC?

- **Solitary thyroid nodules ca risk**
  - Thy 3: 20%
  - tumour >4 cm, atypical cytology (eg cellular pleomorphism), FHx, radiation exposure, age, growth
  - Repeatedly nondiagnostic FNAC: 5%
  - No growth, interval scan

- **MDT discussion**
  - Difficult histology, high risk

- **Patient discussion of alternatives/risks**
What is the appropriate op for **Indeterminate** thyroid nodules?

- Thyroid lobectomy (diagnostic)
  - solitary Thy 3 nodule
  - Thy 3 nodule >4 cm
  - marked atypia (?Thy 4)
  - FHx of thyroid carcinoma
  - Radiation exposure

- **Total Thyroidectomy**
  - Bilateral indeterminate nodules
What is the appropriate op for DTC?

► Papillary

- <1 cm, low-risk, unifocal, intrathyroidal pap ca., no radiation exposure, no neck nodes
  - Lobectomy

- >1 cm
  - Total thyroidectomy

- Thyroid lobectomy or completion

► Follicular

- <1 cm, minimal capsular invasion
  - Lobectomy

- <2 cm low risk
  - Lobectomy only

- Vascular invasion or > 4 cm
  - Total thyroidectomy
Neck Dissection for DTC

- **Clinically or US involved nodes**
  - Anterior Neck (Level 6) dissection
  - Lateral neck: lateral compartmental neck node dissection (favoured over “cherry picking” {lower mortality}) may reduce the risk of recurrence and mortality

- **Prophylactic Level 6 Dissection Controversial**
  - Advanced T3/4 tumours, may improve survival
  - Not for small (T1/2), noninvasive, clinically node-negative PTCs and most follicular ca
  - higher morbidity, recurrent laryngeal nerve injury and transient hypoparathyroidism with no reduction in recurrence.
Surgery for Locally Advanced Disease

► If possible dissect the tumour from the recurrent laryngeal nerve

► **unilateral nerve involvement & extensive extrathyroidal disease**
  - Nerve sacrifice to achieve a curative procedure

► Bilateral nerve involvement
  - A small residue of tumour may be left behind to protect the nerve/s
    - 131I ablation
    - TSH suppression with T4
    - +/- external beam radiotherapy
Management of Aerodigestive Invasion

- Surgery
- 131I RAI ablation
- Ext beam radiotherapy
Role of Postop Staging

1. To provide prognosis
2. To assess risk for disease recurrence and mortality
3. To tailor postoperative adjunctive therapy (RAI therapy and TSH suppression)
4. To determine frequency and intensity of follow-up
5. To enable comparative evaluation of results of treatments
1. **TNM** staging
   - cancer registries & epidemiologic studies
   - does not consider additional independent prognostic variables & risks misclassification of patients.

2. **MACIS**, AGES, AMES, CAEORTC, NTCTCS, U of C, OSU, MSKCC
   - more prognostic staging systems
   - most predictive factors: distant metastases, age & extent of tumour

AGES - Age, Grade, Extent of disease, Size
AMES - Age, Metastasis, Extent of disease, Size
CAEORTC - European Organisation for Research and Treatment of Cancer
Table 1. The TNM system.
(a) Classification according to tumour, nodes and metastases

<table>
<thead>
<tr>
<th>Primary tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT1 Intrathyroidal tumour, ≤1 cm in greatest dimension</td>
</tr>
<tr>
<td>pT2 Intrathyroidal tumour, &gt;1–4 cm in greatest dimension</td>
</tr>
<tr>
<td>PT3 Intrathyroidal tumour, &gt;4 cm in greatest dimension</td>
</tr>
<tr>
<td>pT4 Tumour of any size, extending beyond thyroid capsule</td>
</tr>
<tr>
<td>pTX Primary tumour cannot be assessed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional lymph nodes (cervical or upper mediastinal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0 No nodes involved</td>
</tr>
<tr>
<td>N1 Regional nodes involved</td>
</tr>
<tr>
<td>If possible, subdivide</td>
</tr>
<tr>
<td>N1a Ipsilateral cervical nodes</td>
</tr>
<tr>
<td>N1b Bilateral, midline or contralateral cervical nodes or mediastinal nodes</td>
</tr>
<tr>
<td>NX Nodes cannot be assessed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distant metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0 No distant metastases</td>
</tr>
<tr>
<td>M1 Distant metastases</td>
</tr>
<tr>
<td>MX Distant metastases cannot be assessed</td>
</tr>
</tbody>
</table>
### (b) Papillary or follicular carcinoma staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Under 45 years</th>
<th>45 years and older</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Any T, any N, M0</td>
<td>pT1, N0, M0</td>
</tr>
<tr>
<td>II</td>
<td>Any T, any N, M1</td>
<td>pT2, N0, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pT3, N0, M0</td>
</tr>
<tr>
<td>III</td>
<td></td>
<td>pT4, N0, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any pT, N1, M0</td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td>Any pT, any N, M1</td>
</tr>
</tbody>
</table>

Undifferentiated or anaplastic carcinomas: **All are Stage IV.**
Table 1: 10-year mortality rates for differentiated (papillary or follicular) thyroid cancer.^{10}

<table>
<thead>
<tr>
<th>Stage</th>
<th>10-year cancer-specific mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.7</td>
</tr>
<tr>
<td>II</td>
<td>15.8</td>
</tr>
<tr>
<td>III</td>
<td>30</td>
</tr>
<tr>
<td>IV</td>
<td>60.9</td>
</tr>
</tbody>
</table>
MAICS (Mayo Clinic)

Metastasis, Age, Invasion, Completeness of Resection, Size

- Most reliable staging method to estimate prognosis of PTC
- Assigns scores to the main factors
- Sums score to calculate prognosis
- Children with multiple lung metastases and/or a miliary aspect have excellent long-term prognosis if given adequate treatment.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distant Metastasis: spread of the cancer to areas outside the neck</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Age at the time the tumour was discovered</td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>3.0</td>
</tr>
<tr>
<td>&gt;40</td>
<td>0.08 x age</td>
</tr>
<tr>
<td>Invasion into surrounding areas of the neck as seen by the naked eye</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Completeness of surgical resection (or removal) of the tumour</td>
<td></td>
</tr>
<tr>
<td>Incomplete</td>
<td>1</td>
</tr>
<tr>
<td>Complete</td>
<td>0</td>
</tr>
<tr>
<td>Size of the tumour</td>
<td>0.3x size (cm)</td>
</tr>
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</table>
## MACIS

<table>
<thead>
<tr>
<th>Sum Of MACIS Score</th>
<th>20 year Survival</th>
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<tbody>
<tr>
<td>&lt;6.0</td>
<td>99%</td>
</tr>
<tr>
<td>6.0-6.99</td>
<td>89%</td>
</tr>
<tr>
<td>7.0-7.99</td>
<td>56%</td>
</tr>
<tr>
<td>&gt;8.0</td>
<td>24%</td>
</tr>
</tbody>
</table>
Prognostic Groups

- **Low-risk:**
  - no local or distant metastases
  - complete resection
  - no tumour invasion of locoregional tissues or structures
  - no aggressive histology (e.g., tall cell, insular, columnar cell carcinoma) or vascular invasion
  - no 131I uptake outside the thyroid bed on the first post treatment whole-body RAI

- **Intermediate-risk:**
  - microscopic invasion of tumour into the peri-thyroidal soft tissues
  - cervical lymph node metastases or 131I uptake outside the thyroid bed on the RxWBS after thyroid remnant ablation
  - tumour with aggressive histology or vascular invasion

- **High-risk:**
  - macroscopic tumour invasion
  - incomplete tumour resection
  - distant metastases
  - thyroglobulinemia out of proportion with post treatment scan
Postoperative RAI Remnant Ablation

1. **Recommended**
   - Regional nodal disease, aerodigestive invasion or residual RAI avid disease
   - known distant metastases
   - gross extrathyroidal extension (regardless of size)
   - Primary >4 cm

2. **Recommended for selected patients**
   - 1–4cm thyroid cancers confined to the thyroid with lymph node mets or other risk features
   - age, size, lymph node status & histology intermediate to high risk of recurrence/death

3. **Not Recommended**
   - unifocal cancer <1 cm
   - multifocal cancer when all foci are <1 cm without risk features
Remnant ablation requires TSH stimulation

- TSH >30mU/L for RAI uptake in tumours
- Withdrawal of T3
- Exogenous TSH
Role of human recombinant TSH (thyrotropin) (rhTSH)

- for patients
  - unable to tolerate hypothyroidism (underlying co-morbidities)
  - unable to generate an elevated TSH (pituitary disease)
  - in whom a delay in therapy might be deleterious

- equally effective, with QOL

- ablation rates with 50 mCi = 100 mCi rates when rhTSH used but with 33% in whole-body irradiation

- Used in the UK with the world wide shortage of T3
RAI Ablation Complications

- Salivary gland damage: sialadenitis, dry mouth, dental caries, loss of taste
- Nasolacrimal duct obstruction/tearing
- Secondary malignancies (dose related)
  - Risk of second malignancies: 1.19
  - Risk of leukaemia: 2.5
  - Risk of breast cancer: ? screening bias, RAI therapy or other factors

- Reduce
  - Laxatives: radiation exposure of the bowel
  - Oral hydration will reduce exposure of the bladder and gonads
RAI: Gonadal fn & breast feeding

► Women
  □ 25% Temporary amenorrhea/oligomenorrhea
  □ Should not be under go treatment if pregnant
  □ Pregnancy should be postponed for 6-12 months
  □ Radioactive iodine should not be given to breast feeding women.
  □ Deferred until 6-8 week post breast-feeding
  □ ? Dopaminergic agents to breast exposure in recently lactating women

► Men
  □ Temporary sperm counts
  □ Permanent male infertility is unlikely with a single ablative activity of RAI
  □ Sperm banking in men who receive > 2 RAI treatments
  □ Fertility and risks of miscarriage or congenital abnormalities in subsequent pregnancies are not changed with moderate RAI activities
Adjunctive external beam irradiation or chemotherapy?

- **External beam irradiation (EBR).**
  - Palliative treatment for locally advanced, unresectable disease
  - Patients > 45 with
    - Grossly visible extrathyroidal extension at the time of surgery
    - Likelihood of microscopic residual disease,
  - Patients with gross residual tumour in whom further surgery or RAI would be ineffective

- **Chemotherapy**
  - No data to support the use of adjunctive chemotherapy in the management of DTC.
  - Doxorubicin may act as a *radiation sensitizer* and could be considered for patients with locally advanced disease undergoing external beam radiation
Thyrotropin (TSH) suppression therapy?

- TSH suppression prevents major adverse events
- No benefit stage I disease
  - Total thyroidectomy, given in our MDT
- Survival TSH 0.1 - 0.5 stage II disease
- Survival TSH <0.1mU/L in patients with Stage III/IV

Adverse effects of TSH suppression

- Subclinical thyrotoxicosis: exacerbation of angina, risk of atrial fib, risk of osteoporosis

Long-term Management

Accurate surveillance for possible recurrence

- **Low risk of recurrence**
  - less aggressive follow up
  - Normal life expectancy (with total thyroidectomy and 131I ablation)

- **High risk of recurrence: monitor more closely**
  - life expectancy 60% of that in the general population (varies depending upon tumour features)

- **Patients with persistent/recurrent disease**
  - offered treatment to cure or to delay future morbidity/mortality.

Monitor thyroxine suppression or replacement therapy, to avoid over aggressive therapy or under replacement
Serum thyroglobulin (Tg) assays

Monitor for residual/recurrent disease
- 6 – 12 monthly
- Low risk, total thyroidectomy, post op RAI, if –ve Tg, test yearly
- Monitor change in levels with time
- Highest sensitivity/specificity with T3/4 withdrawal or rhTSH stim
- Tg<0.5 ng/mL 99.5% disease free

Pitfalls
- **Use same lab:** 2x variation in tests
- Fail to detect small amounts of residual ca
- anti-Tg antibodies false levels
- defective or absent Tg production
- **Difficult to interpret if no post op RAI ablation**
  - Better to use US in this group
Ultrasound Neck Post op

► 6–12 months
  - then periodically dependent patient risk & Tg status

► suspicious lymph nodes > 5–8mm
  - FNAC
  - Tg measurement in the needle washout (?UK)

► suspicious lymph nodes < 5–8mm
  - followed without biopsy
  - consider if size
Diagnostic Whole body Radioactive Iodine Uptake *Scan* (Dx WBS)

(RAI = Radioactive Iodine Ablation)
(RxWBS = Post Treatment (3-6 days) Whole body Radioactive Iodine Uptake *Scan*)
(DxWBS = Diagnostic Whole Body Radioactive Iodine Uptake *Scan*)

1. **Low-risk patients**
   - undetectable Tg on T4 (-ve antiTg ab) and –ve US)
   - *do not require* routine DxWBS (after the first RxWBS)

2. **Intermediate or high risk** of persistent disease
   - DxWBS 6–12 months after remnant ablation
18FDG-PET
(NOT IN LOW RISK PATIENTS!)

1. Disease localization in Tg-positive, RAI –ve patients
2. Initial staging & follow-up of
   - invasive or metastatic Hurthle cell ca
   - high-risk poorly diff. Ca
3. Measurement of response following external beam irradiation, surgical resection, embolisation or systemic therapy
Management of Metastatic Disease

- **Surgery for locoregional disease** (lymph nodes >0.8 cm)
  - comprehensive or selective ipsilateral +/- Level VI dissection
    - (preservation of XI, IJV & SCM)
    - May be limited by previous neck dissection and external beam radiotherapy
    - NOT “berry picking”
  
- **131I therapy for RAI-avid disease**

- **external beam radiation**

- **watchful waiting with patients with stable or slowly progressive asymptomatic disease**

- **experimental trials** (significantly progressive macroscopic refractory disease)

- **radiofrequency or ethanol ablation, chemo-embolisation**
Role of external beam radiation therapy?

- unresectable gross residual or recurrent cervical disease
- painful bone metastases
- metastatic lesions in critical locations, not amenable to surgery, likely to result in fracture, neurological, or compressive symptoms
- vertebral, CNS, Mediastinal or Pelvic metastases
US Reports

- There are multiple nodules in the thyroid gland
- There are multiple nodules with a dominant nodule
- There are multiple nodules with a 2 cm dominant nodule
- There are multiple nodules with a 3 cm nodule with no suspicious features
- There is a solitary nodule with suspicious features (micro-calcification) and an FNAC was performed
US

- Nick Reading
- Curtis Offiah